Preface

Since the first edition of this book dedicated to differential display (DD) technology was published in 1997, we have witnessed an explosive interest in studying differential gene expression. The gene-hunting euphoria was initially powered by the invention of DD, which was gradually overtaken by DNA microarray technology in recent years. Then why is there still the need for second edition of this DD book? First of all, DD still enjoys a substantial lead over DNA microarrays in the ISI citation data (*see* Table 1), despite the hundreds of millions of dollars spent each year on arrays. This may come as a surprise to many, but to us it implies that many of the DNA microarray studies went unpublished owing to their unfulfilled promises ***(1)***. Second, unlike DNA microarrays, DD is an "open"-ended gene discovery method that does not depend on prior genome sequence information of the organism being studied. As such, DD is applicable to the study of all living organisms—from bacteria, fungi, insects, fish, plants, to mammals—even when their genomes are not sequenced. Second, DD is more accessible technically and financially to most cost-conscious "cottage-industry" academic laboratories. So clearly DD still has its unique place in the modern molecular biological toolbox for gene expression analysis.

The second edition of *Differential Display Methods and Protocols* consists of a varying collection of chapters that highlight both recent methodological refinements (Chapters 1–8) and some of the fine examples of DD applications in recent years. Most of the published DD screenings in the past took a shotgun approach, by using only a limited number of primer combinations, in which only one gene was identified and characterized. This gave DD an image of low tech, low throughput, and low gene coverage. With the mathematical model for DD now solved (Chapter 1), a genome-wide comprehensive DD screening has become possible. The key to the success of high-throughput and high coverage of DD platform lies in a transition from radioactive labeling to fluorescence digital readout, as well as automated liquid handling of hundreds of DD PCR reaction setups combined with capillary electrophoresis (Chapters 2 and 4). A prototype computer program has been developed to automatically allow positive band identification from an FDD image (Chapter 7). Restriction fragment-based DD screenings offer an alternative to traditional DD and has a potential of linking any cDNA fragment directly to a given gene once the se-

Table 1
ISI Citation List [a]

Methods	Citation No.	Original publication
Differential display	3597	SCIENCE 257 (5072): 967-971, 1992
DNA microarrays	2269	SCIENCE 270 (5235): 467-470, 1995
Oligo arrays	740	SCIENCE 274 (5287): 610-614, 1996

[a]ISI Search ***(2)***.

quence information of all transcripts becomes available (Chapters 3, 4, and 8). Efforts to combine DD and DNA microarrays by reducing the complexity of cDNA probes while increasing the sensitivity of detection has been made successfully (Chapter 6). A DD approach has also been formulated to detect prokaryotic mRNA expression (Chapter 5).

Obviously, no matter which gene discovery methodologies one chooses to use, ultimately it will be the functional characterizations of each isolated gene, by genetic, cell biological and biochemical methods, that will likely provide the real proof (or disproof) of the relevance of the genes to a biological system under investigation. In a preface to a methods book on protein purification, Dr. Arthur Kornberg had once quoted an admonition of Efraim Racker, "Don't waste clean thinking on dirty enzymes," to illustrate the importance of good biochemical practice at the core of enzymology. A similar doctrine, "Don't waste clear thinking on dirty data," will certainly continue to help to produce better quality of science in the field of gene expression analysis over the next ten years. With this principle as a guiding light, we are extremely pleased to be able to demonstrate to our readers the power of DD technology, which is best substantiated by the genes it uncovered. Given the limit in scope and space of this book, here we can only showcase a few out of the thousands of successful DD applications published. The elegant studies described in Part II of this book have led to the discovery of many important genes involved in viral infection, Prion disease, cancer, ovulation, circadian clock, floral color, transcription repression, gene silencing, mRNA polymorphism, and protein–RNA interaction. The hallmark of a successful gene hunting expedition common to all of these DD applications is that these studies did not end with gene listing, but rather that finding the gene(s) by DD only served as a beginning of a long and often difficult scientific pursuit. We certainly hope that their footsteps will

be followed as by all those seriously contemplating a fruitful gene-hunting expedition in the future. Happy gene hunting!

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References

1. Liang, P. and Pardee, A. B. (2003) Analysing differential gene expression in cancer. *Nature Reviews Cancer* **3,** 869–876.
2. ISI Search conducted on Dec 30, 2004 at Thompson Scientific, ISI Web of Knowledge. www.isinet.com.